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10/563,726	06/30/2006	Mark C. Poznansky	62063(51588)	1191

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EXAMINER	
ROOKE, AGNES BEATA	
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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/563,726	POZNANSKY ET AL.	
	Examiner	Art Unit	
	Agnes B. Rooke	1656	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *20 September 2007*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-124* is/are pending in the application.

4a) Of the above claim(s) *18-28 and 45-124* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-17 and 29-44* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *06 January 2006* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *March 13,2006*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

Application Status

1. Applicant's election with traverse of Group VI (claims 29-44, SEQ ID NO:3) is acknowledged. Applicants' traversal is on the ground that the subject matters of Groups VI and I represent different embodiments of a single inventive concept for which a single patent should issue. Also, Applicants state that a sufficient search and examination with respect to the subject matter of the claims of Groups VI and I can be made without a serious burden. Further, Applicants state that that it would not be unnecessary burden on the examiner to search and examine Groups VI and I at the same time because of the powerful search engines and data bases available to the examiner.

Examiner acknowledges Applicants' arguments and rejoins Group I with Group VI as a single inventive concept. Thus, the Restriction Requirement mailed on 6/20/2007 is withdrawn in part.

Claim Disposition

2. Claims 1-124 are pending. Claims 1-17 and 29-44 are under examination with reference to SEQ ID NO:3. Claims 18-28 and 45-124 are withdrawn from further consideration pursuant to 37 CFR 1.12(b), as being drawn to a non-elected invention, there being no allowable generic or linking claim.

Priority

3. This application claims priority to 371 of PCT/US04/21725 filed on 07/07/2004, which claims priority to 60/485,550 filed on 07/07/2003. The Applicants are awarded the benefit for those documents.

Specification

4. The specification is objected to because of the following informalities:

a) The priority information on the first page of the specification must match the data disclosed on the Bib Data Sheet. For example: "This application is a 371 of PCT/US04/21725 filed on 07/07/2004 which claim benefit to 60/485,550 filed on 07/07/2003.

b) The specification is also objected to because it contains an embedded hyperlink and/or other form of browser-executable code. Applicant is required to delete the embedded hyperlink and/or other form of browser-executable code. See MPEP § 608.01. See page 56, line 31, for example. It is suggested that <http://> is deleted.

c) The specification is objected to because the Brief Description of the Drawings section and the drawings depict Figure 12A to 12C only that refers to Figure 12. Also, the drawings depict Figures 13A to 13 B where the specification refers to only Figure 13; also drawings depict Figures 14 A to 14C where the specification refers only to Figure 14; further, drawings refer to Figures 15A to 15B where the specification refers only to Figure 15; in addition, drawings depict Figures 16 A to 16B where the specification refers only to Figure 16.

d) On page 14 of the Figures, in the Detailed Results section, the sequences listed lack SEQ ID NOs or Accession numbers.

Therefore, proper correction of the above is required.

Drawing

5. The drawings submitted on 01/06/2006 are accepted by examiner.

Claim Objection

6. The claims are objected for the following reasons:

a) Claim 29 is objected to because the full spelling of the name of a protein, such as "HSP" has to be provided in the first instance in the claim.

b) Claims 1-17 are objected to because the nomenclature as in reference to the "HSP90" or "hsp90" family should be constant.

c) Claims 9, 29, and 41 are objected to because they refer to non-elected subject matter and only SEQ ID NO:3 that is HSP90α was elected.

d) Claims 13-17 are objected to because they depend from a rejected based claim.

e) For clarity purposes claim 1 is objected to because it is not clear whether the HSPLP is also "isolated." Therefore, proper correction is required.

Information Disclosure Statement

7. The Information Disclosure Statement filed on 03/13/2006 has been received and entered. The references cited on the PTO-1449 Form have been considered by the examiner and a copy is attached to the instant Office action.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter, which the applicant regards as his invention.

8. Claims 12 and 29-44 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 12 is indefinite because it is not clear what is defined by "a stressed or a non-stressed cell" thus further characterization is the claim is required.

Claims 29-44 are rejected because it is not clear what is specifically claimed as being the elected invention since it is ambiguous with respect to HSPLP, L-plastin, or LPLP, and also similar to fragments thereof, see specification [0013], for example. The elected SEQ ID NO:3 represents only **HSP90α**, and does not specifically represent other proteins, such as HSPLP, L-plastin, or LPLP, fro example.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

9. Claims 1-17 and 29-44 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Claims 1-8 and 10-17 are directed to any isolated HSP or HSPLP absent any structural limitation

In addition, the instant invention claims a method of promoting fugetaxis of migratory cells in a subject comprising administering to a subject the HSP, HSPLP, L-plastin, or LPLP (these are essentially fragments of HSP) of SEQ ID NO:3 or a fragment thereof, in an amount effective to promote fugetaxis of migratory cells away from a specific site in a subject. Thus, the Applicants claim any HSP protein (where the elected SEQ ID NO:3 refers to HSP90α protein only). Further, Applicants claim any fragment of HSP protein, where the fragment can be represented by any dipeptide, see claim 9, for example; wherein the fragment is not specified in the claims as presented.

Therefore, the skilled artisan cannot envision the detailed chemical structure of any HSP, HSPLP, L-plastin or LPLP, and fragments with respect to SEQ ID NO:3 or any HSP, HSPLP, L-plastin or LPLP because SEQ ID NO:3 has over 700 amino acid residues and there is no indication of what position(s) corresponds to the recited HSP,

HSPLP, L-plastin or LPLP with respect to the variation needed in SEQ ID NO:3 with respect to the variation needed in SEQ ID NO:3. Thus, the claims lack written description.

Additionally, the instant specification does not demonstrate possession of said fragments. The specification does not exemplify, for example, relevant fragments of SEQ ID NO:3 or relevant fragments of HSP proteins as a whole. No correlation is made between the structure and function, for example, the identification of domains or conserved regions of SEQ ID NO:3 are unknown. Also, examples of such fragments are not disclosed in the instant application and appear to be pertinent to the claimed invention.

A representative number of species means that the species, which are adequately described, are representative of the entire genus. The written description requirement for a claimed genus may be satisfied through sufficient description of a representative number of species by actual reduction to practice, disclosure of drawings, or by disclosure of relevant identifying characteristics, for example, structure or other physical and/or chemical properties, by functional characteristics coupled with a known or disclosed correlation between function and structure, or by a combination of such identifying characteristics, sufficient to show the applicant was in possession of the claimed genus.

Accordingly, in the absence of sufficient recitation of distinguishing identifying characteristics, the specification does not provide adequate written description of the claimed genus. For example, the claimed genus of fragments of HSP in general could

include non-functional proteins or proteins with a different function than the one described for SEQ ID NO:3. Therefore, the genus of claimed polypeptides encompasses widely variant species. Based on the unlimited variations contemplated, one skilled in the art would at best expect a protein that is different or at worst a protein that is not functional.

Vas-Cath Inc. v. Mahurkar, 935 F.2d 1555, 1563-64, 19 USPQ2d 1111, 1117 (Fed. Cir.1991), states that "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in *possession of the invention*. The invention is, for purposes of the 'written description' inquiry, *whatever is now claimed*" (See page 1117). The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed" (See *Vas-Cath* at page 1116). The skilled artisan cannot envision the detailed chemical structure of the encompassed genus of polypeptides, and therefore, conception is not achieved until reduction to practice has occurred, regardless of the complexity or simplicity of the method of isolation. Adequate written description requires more than a mere statement that it is part of the invention and reference to a potential method of isolating it. The compound itself is required. *See Fiers v. Revel, 25 USPQ2d 1601 at 1606 (CAFC 1993).*

Therefore, for all these reasons the specification lacks adequate written description, and one of skill in the art cannot reasonably conclude that the applicant had possession of the claimed invention at the time the instant application was filed.

10. Claims 1-17 and 29-44 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for the protein set forth in SEQ ID NO:3, does not reasonably provide enablement for any HSP, and any HSPLP, or L-plastin, or LPLP. In addition, the claims are not enabled for any fragments thereof a recited in fro example in claim 29. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to practice the invention commensurate in scope with these claims.

The enablement requirement refers to the requirement that the specification describe how to make and how to use the invention. There are many factors to be considered when determining whether there is sufficient evidence to support a determination that a disclosure does not satisfy the enablement requirement and whether any necessary experimentation is undue. These factors include, but are not limited to: Quantity of Experimentation Necessary; Amount of direction or guidance presented; Presence or absence of working examples; Nature of the Invention; State of the prior art and Relative skill of those in the art; Predictability or unpredictability of the art and Breadth of the claims (see *In re Wands, 858 F.2d at 737, 8 USPQ2d at1404 (Fed. Cir. 1988)*. The factors most relevant to the instant invention are discussed below.

The amount of experimentation required to practice the claimed invention is undue as the claims encompass an unspecified number of fragments of SEQ ID NO:3 or any fragment of HSP protein that promotes fugetaxis. Further, experiments presented in the specification does not disclose SEQ ID NO:3 or any fragments of it. The instant specification does not demonstrate or provide guidance as to what the structure of the

protein will be once modified or if said protein will be functional or exhibit the same properties or characteristics as the native protein. Further, the unspecified fragments may not function as disclosed and thus, the claims encompass variants/fragments that may not have any biological activity. Due to the large quantity of experimentation necessary to generate the infinite number of variants/fragments recited in the claims and possibly screen same for activity and the lack of guidance/direction provided in the instant specification, this is merely an invitation to the skilled artisan to use the current invention as a starting point for further experimentation. Thus, undue experimentation would be required for a skilled artisan to make and/or use the claimed invention commensurate in scope with the claims.

Predictability of which potential changes can be tolerated in a protein's amino acid sequence and obtain the desired activity requires a knowledge of and guidance with regard to which amino acids in the protein's sequence, if any, are tolerant of modification and which are conserved (for example, expectedly intolerant to modification), and detailed knowledge of the ways in which the protein's structure relates to its function. In addition, one skilled in the art would expect any tolerance to modification for a given protein to diminish with each further and additional modification, for example. For example, various sites or regions directly involved in binding activity and in providing the correct three-dimensional spatial orientation of binding and active sites can be affected (see Wells, Biochemistry, vol. 29, pages 8509-8517, 1990). The instant specification provides no guidance/direction as to which regions of the protein would be tolerant of modifications and which would not, and it provides no working

examples of any fragment/variant sequence that is encompassed by the claims. The skilled artisan would recognize the high degree of unpredictability that all the fragments/variants encompassed in the claims would retain the recited function.

The state of the prior art provides evidence for the high degree of unpredictability as stated above. Seffernick et al. (J. Bacteriology, vol. 183, pages 2405-2410, 2001) disclose two polypeptides having 98% sequence identity and 99% sequence identity, differing at only 9 out of 475 amino acids (page 2407, right column, middle and page 2408, Fig. 3). The polypeptides of Seffernick et al. are identical along relatively long stretches of their respective sequences (page 2408, Fig. 3), however, these polypeptides exhibit distinct functions. The modifications exemplified in the Seffernick et al. reference is small compared to those contemplated and encompassed by the claimed invention (see page 21 of the specification and claim 3, for example).

The specification lacks adequate guidance/direction to enable a skilled artisan to practice the claimed invention commensurate in scope with the claims. The amino acid sequence of a protein determines its structural and functional properties, and predictability of what fragments can be tolerated in a protein's sequence and result in certain activity, which is very complex, and well outside the realm of routine experimentation, because accurate predictions of a protein's function from mere sequence data are limited, therefore, the general knowledge and skill in the art is not sufficient, thus the specification needs to provide an enabling disclosure.

The working examples provided do not rectify the missing information in the instant specification pertaining to the claimed variant. The nature and properties of this

claim is difficult to ascertain from the examples provided as one of skill in the art would have to engage in undue experimentation to construct the variants of the claimed invention and examine the same for function, since such fragments of HSP or SEQ ID NO:3 are not discussed.

The specification does not provide support for the broad scope of the claims, which encompass an unspecified amount of variants/fragments of HSP protein or SEQ ID NO:3. The claims broadly read on any fragment thereof for the given SEQ ID NO:3 of HSP. The issue in this case is the breath of the claims in light of the predictability of the art as determined by the number of working examples, the skill level artisan and the guidance presented in the instant specification and the prior art of record. This make and test position is inconsistent with the decisions of *In re Fisher, 427 F.2d 833, 839, 166 USPQ 18, 24 (CCPA 1970)* where it is stated that "...scope of claims must bear a reasonable correlation to scope of enablement provided by the specification to persons of ordinary skill in the art...". Without sufficient guidance, determination of having the desired biological characteristics is unpredictable and the experimentation left to those skilled in the art is unnecessarily and improperly extensive and undue. See *In re Wands, 858 F.2d at 737, 8 USPQ2d at 1404 (Fed. Cir. 1988)*. Therefore, absent direction/guidance regarding whether the structure of the different fragments of HSP protein or SEQ ID NO:3 can tolerate the modifications contemplated, a non-functional protein may result and one of skill in the art would not be able to practice the claimed invention commensurate in scope with the claims. In addition, absent direction/guidance

regarding the different fragments of HSP or SEQ ID NO:3 polypeptides, one of skill in the art would not be able to make the desired composition.

Thus, for all these reasons, the specification is not considered to be enabling for one skilled in the art to make and use the claimed invention as the amount of experimentation required is undue, due to the broad scope of the claims, the lack of guidance and working examples provided in the specification and the high degree of unpredictability as evidenced by the state of the prior art, attempting to construct and test variants of the claimed invention would constitute undue experimentation. Making and testing the infinite number of possible variants to find one that functions as described is undue experimentation. Therefore, applicants have not provided sufficient guidance to enable one of skill in the art to make and use the claimed invention in a manner that reasonably correlates with the scope of the claims, to be considered enabling.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

11. Claims 1-7 and 9- rejected under 35 U.S.C. 102(b) as being anticipated by WO/52791 (07/2001).

Srivastava teaches pharmaceutical compositions comprising peptide-binding fragments of heat shock proteins (HSPs) and non-covalent complexes of peptide-binding fragments of HSPs. See Abstract.

Claim 50, on page 80, and pages 10-12 of Srivastava teach SEQ ID NO:5, that has 100% identity to the instant SEQ ID NO:3. (see instant claims 1-7 and 9). The claims are anticipated because the elected SEQ ID NO:3 is HSP90α (instant claims 7 and 9) and where the protein belongs to HSP90 families (instant claims 5 and 6). Although, the reference does not teach the fugetactic activity per se, it would be inherent property because the structure is disclosed by the reference.

In addition, claims 2-4 are included in this rejection because Srivastava teaches different fragments of HSP proteins and thus these proteins will have different molecular weight, for example.

Conclusion

12. No claims are allowable.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Agnes Rooke whose telephone number is 571-272-2055. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Kathleen Kerr Bragdon can be reached on 571-272-0931. The fax phone number for the organization where this application or proceeding is assigned is 571-272-8300. Information regarding the status of an application may be obtained from the

Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information about the PAIR system, see http://pair-direct.uspto.gov. Should you have any questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197.

AR

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PRIMARY EXAMINER